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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/901,372	07/09/2001	Sarah Black	SH-1	6590

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EXAMINER	
MARSCHEL, ARDIN H	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 06/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/901,372	BLACK ET AL.	
	Examiner	Art Unit	
	Ardin Marschel	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *6/9/04 (Withdrawl of allowability)*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2, 6-9, and 11-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2, 6-9, and 11-21* is/are rejected.

7)☒ Claim(s) *2, 6-9, and 11-21* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892) (2 sheets)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The withdrawl from Issue Notice, mailed 6/9/04, is hereby acknowledged. Upon reconsideration of the instant application, the following rejections and/or objections newly applied. They constitute the complete set presently being applied to the instant application.

LACK OF ENABLEMENT

Claims 2, 6-9, and 11-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a prima facie case are discussed below.

A possible interpretation of the X-ray crystallography limitation practice in instant claim 2 is that the entire structure inclusive of first and second microtubules as well as a multiplicity of microtubule-associated proteins are positioned and analyzed via said X-ray crystallography as set forth in the last 3 lines of instant claim 2. No specific guidance has been found as filed for the formation of a suitable crystal for such a complex structure so as to obtain positional/pattern information as is instantly claimed. It is additionally set forth that the literature supports the unpredictability of formation of crystals for X-ray crystallography practice that are suitable for atomic coordinate determinations even for single proteins. See Drenth at page 1, lines 1-7, in the section entitled "1.2 Principles of Protein Crystallization" wherein the trial and error status of this "underdeveloped area" is described. Additionally, Robert Service in Science, Vol. 298, pages 948-950 (2002), well after the instant filing date summarizes the production of 3-dimensional structures as being a "Trickle" compared to massive efforts directed at such structural determination. Thus, it is reasonably deemed unpredictable as well as undue experimentation to obtain a suitable crystal for X-ray crystallography positioning or patterning of molecular structure without the conditions for forming such a crystal specifically set forth. No such conditions have been set forth in the instant application as filed.

Similarly, claim 6 is directed to mass spectroscopy determination of microtubule/associated protein compositions which is well known to be a process wherein disruption of a sample is a required step in such a process thus destroying intermolecular positioning and patterns as well as most intramolecular bonds as well. Thus, it would be unpredictable as well as undue experimentation to utilize mass spectrometry as in instant claim 6 for determining composition of microtubules and associated proteins so as to accomplish the instantly claimed positioning and patterning of such complex structures.

A possible interpretation of instant claim 7 is that a Qbit pattern is a specific data structure which defines the positions and patterns as instantly claimed. No guidance has instantly been found for formation of such a pattern. Thus, it would be unpredictable as well as undue experimentation to determine such a pattern as in instant claim 7 for determining composition of microtubules and associated proteins so as to accomplish the instantly claimed positioning and patterning of such complex structures.

In claims 8 and 9 secondary protein messengers as determined regarding transport/destinations. No guidance or suggestion of what such protein secondary messengers are meant or interact with the claimed microtubule/associated proteins structure and thus it would be undue experimentation as well as unpredictable to search through the myriad of cellular proteins to find one or more such messengers.

A possible interpretation of instant claims 11 and 12 is that intact cells are to be imaged in order to obtain the positions and patterns as specific data as instantly

claimed. No guidance has instantly been found for what is to be performed to image such intact cells in order to obtain such positions and patterns. Thus, it would be unpredictable as well as undue experimentation to determine such a pattern as in instant claims 11 and 12 for determining composition of microtubules and associated proteins so as to accomplish the instantly claimed positioning and patterning of such complex structures.

A possible interpretation of instant claims 2, 6-9, and 11-21 is that intact structures which are present in cells are sampled in order to practice respective parts (a) of the instant independent claims. No guidance has instantly been found for what is to be performed to image such intact cell structures in order to obtain such positions and patterns. It is well known that internal cell structures, especially complex ones, are extremely difficult, if not impossible, to isolate intact for study without at least some disruption. This disruption is unpredictable unless very controlled and tested conditions are utilized, especially since living organism status is apparently meant to be determined therefrom. Thus, it would be unpredictable as well as undue experimentation to determine such a pattern as in all of the instant claims for determining composition of microtubules and associated proteins so as to accomplish the instantly claimed positioning and patterning of such complex structures.

Instant claims 17-21 additionally are directed to the treating of living organisms as a step that is apparently to be performed with the imaging of the instantly claimed method steps along with status determination. Such treatments are unpredictable and require undue experimentation unless accompanied by some guidance as to what is

meant to be accomplished, especially regarding instantly claimed microtubule/associated protein structures. On page 11, fourth full paragraph, for example, several correlations are asserted, however, without any guidance as to what treatment amounts, times, etc. would predictably result in desired affects. Thereafter several Patent documents are cited regarding treatments for various disease states, however, again without any guidance as to what particular correlation exists for such disease states with microtubule/associated protein patterns are predictive of the usefulness therefrom of such treatments.

It is additionally noted that numerous Patent documents are cited in the instant specification, however, enablement of the above cited practices has not been found to specifically result in the practice of the instantly set forth claims regarding the issues specifically described above.

VAGUENESS AND INDEFINITENESS

Claims 2, 6-9, and 11-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Steps (c), (d), (e), and (f) of the instant independent claims mix the determination of positions and patterns therein without defining any relationship therebetween. For example, instant claim 2, part (e), compares positions with historic phenotypic data whereas part (f) compares patterns without any reference to the position comparison in part (e) except for a wherein clause in the last 3 lines of claim 2, part (f), which is not specifically related to the status determination in the first 4 lines of

step (f). The relationship between these differently worded steps is unclear and causes the instant claims to be vague and indefinite as to what is meant by these unconnected limitations. Clarification via clearer claim wording is requested. Claims which depend from claim 17 are also included herein due to their dependence.

PRIOR ART

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 2, 7-9, and 14-16 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Rice et al. [Nature 402:778 (1999)].

Rice et al. describes the interaction of kinesin motor protein with microtubules as summarized in the abstract and throughout the reference. This is reasonably interpreted as a determination of a status of such structures within a living organism. It is noted that the above listed instant claims do not limit what specific status aspect or aspects are being determined within the scope of the instant claims. The kinesin motor protein interacts with microtubules for its motor function and thus qualifies as a microtubule associated protein. Microtubules and kinesin was obtained via various cellular samples as set forth in the "Methods" section of Rice et al. on page 783 as step (a) of instant claim 2. The positions and patterns of a multiplicity of kinesin proteins and microtubules were described and imaged as set forth in the sections entitled "Structural changes visualized by cryo-EM", "ATPase kinetics of G234A and E236A mutants", etc.

on pages 780-783 also including Figure 4 which specifically shows images as instantly claimed in claim 2, parts (b), (c), and (d). The comparison of the positioning of the above kinesin/microtubule system with historic phenotypic data is described in the reference on page 783 in the section entitled "Comparison with other motors" wherein data from other motor types for previous (historic) publications is described both regarding similarities as well as differences. The last three lines of instant claim 2 requires that positions of microtubules and a multiplicity of microtubule associated proteins must be determined by X-ray crystallography. The imaging and thus the positions of these materials with X-ray crystallography usage is disclosed relating to Figure 4 of the reference which utilizes X-ray crystallography for positioning kinesin as described on page 780, second column, second full paragraph wherein the crystal structure is utilized for said kinesin positioning. Figure 1 on page 779 shows the X-ray crystallography structure of a kinesin. Instant claim 7 is included hereinunder as being rejected because the Qbit pattern limitation which is cited therein is reasonably interpreted as a generic pattern of data output from an analysis. MacCrisken (P/N 4,730,348) is cited here only to supply evidence that output data is Qbit data as described therein in column 16, lines 30-36. X-ray crystallography is such an output data set as described above for kinesin structure. Instant claim 8 is also rejected hereinunder because Rice et al. on pages 781-782 in the section entitled "ATPase kinetics of G234A and E236A mutants discloses the speeds of both ATP hydrolysis as well as ADP release (destinations as in instant claim 9) as well as corresponding conformation changes in a microtubule/kinesin assembly. ATP and ADP are

reasonably interpreted as a secondary energy messengers for protein conformation change. Instant claims 14-16, directed to digitized data production for imaging is rejected also hereinunder because the section entitled "Cryo-EM and image analysis" on page 784 of Rice et al. references Sosa et al. [Cell 90:217 (1997)] regarding imaging. Sosa et al. is supplied as evidence that the imaging of Rice et al. is digital because Sosa et al. states such digital imaging on page 223, second column, section entitled "Image Analysis".

Claim 12 is rejected under 35 U.S.C. 102(b) as being clearly anticipated by Scherson et al. [Journal of Cell Biology 99:425 (1984)].

Scherson et al. summarizes the microtubule/MAPs living organism status of calf brain via dynamic imaging as summarized in the title and abstract as also in instant claim 12, parts (b) – (e). Figure 5 with associated discussion shows both labeled MAPs (microtubule associated protein) as well as labeled microtubule images. These were prepared from cellular material as described therein in the Figure 5 legend as also required in instant claim 12, part (a). The reference compares historic phenotypic data from other studies in the section entitled "DISCUSSION" on pages 431-433 as required also steps (e) and (f) of instant claim 12 thus anticipating said claim 12.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 12, 14, and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Scherson [Journal of Cell Biology, Vol. 99:425 (1984)]; taken in view of Bacus et al. (P/N 4,998,284).

Scherson et al. has been summarized above regarding the basic instant invention but does not describe digitizing the dual color images therein obtained.

Bacus et al. is directed to dual color imaging of specimens for staining and analysis as summarized in the title and abstract. The disclosure of Bacus et al. as a whole goes into details of such a methodology and specifically describes digital image processing in column 6, lines 33-46, as required in instant claims 14 and 15. Bacus et al. motivates the imaging methodology therein for cellular specimen analysis in column 1, line 25, through column 3, line 54, as inexpensive and easily adjustable to improve cellular analysis as also instantly claimed.

Thus, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice digital image processing as motivated by Bacus et al. for cellular specimen imaging and analysis as in Scherson et al. to result in the digital imaging embodiments of the above listed instant claims.

INFORMALITIES

The disclosure is objected to because of the following informalities:

The following misspellings appear to be present in the below listed claims.

Claim 2, line 4: "microtuble"

Claim 2, line 8: "mircotubule"

Claim 2, line 9 (twice): "microtuble"

Claim 2, line 14 (twice): "microtuble"

Claim 6, line 4: "microtuble"

Claim 6, line 8: "mircotubule"

Claim 6, line 9 (twice): "microtuble"

Claim 6, line 14 (twice): "microtuble"

Claim 6, line 21: "compositons"

Claim 7, line 4: "microtuble"

Claim 7, line 8: "mircotubule"

Claim 7, line 9 (twice): "microtuble"

Claim 7, line 14 (twice): "microtuble"

Claim 8, line 4: "microtuble"

Claim 8, line 8: "mircotubule"

Claim 8, line 9 (twice): "microtuble"

Claim 8, line 14 (twice): "microtuble"

Claim 9, line 4: "microtuble"

Claim 9, line 8: "mircotubule"

Claim 9, line 9 (twice): "microtuble"

Claim 9, line 14 (twice): "microtuble"

Claim 11, line 4: "microtuble"

Claim 11, line 8: "mircotubule"

Claim 11, line 9 (twice): "microtuble"

Claim 11, line 14 (twice): "microtuble"

Claim 12, line 4: "microtuble"

Claim 12, line 8: "mircotubule"

Claim 12, line 9 (twice): "microtuble"

Claim 12, line 14 (twice): "microtuble"

Claim 13, line 4: "microtuble"

Claim 13, line 8: "mircotubule"

Claim 13, line 9 (twice): "microtuble"

Claim 13, line 14 (twice): "microtuble"

Claim 14, line 4: "microtuble"

Claim 14, line 8: "mircotubule"

Claim 14, line 9 (twice): "microtuble"

Claim 14, line 14 (twice): "microtuble"

Claim 15, line 4: "microtuble"

Claim 15, line 8: "mircotubule"

Claim 15, line 9 (twice): "microtuble"

Claim 15, line 14 (twice): "microtuble"

Claim 17, line 4: "microtuble"

Claim 17, line 8: "mircotubule"

Claim 17, line 9 (twice): "microtuble"

Claim 17, line 14 (twice): "microtuble"

Claim 21 is single spaced which is improper. Claims must be submitted either as 1 ½ or double spaced in format.

Claim objections are listed on the enclosed PTO Form 326 inclusive of dependent claims which also are objected to, however, due to their dependence from claims which contain the above objections.

Appropriate correction is required.

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the Central PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The Central PTO Fax Center number is (703) 872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ardin Marschel, Ph.D., whose telephone number is (571) 272-0718. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (571) 272-0722.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instrument Examiner, Tina Plunkett, whose telephone number is (571) 272-0549.

June 25, 2004

ARDIN H. MARSCHEL
PRIMARY EXAMINER

6/25/04